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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,552	08/02/2001	Hideakira Yokoyama	0020-4883P	4627
2292	7590	02/23/2005	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			KRASS, FREDERICK F	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/890,552	YOKOYAMA ET AL.
	Examiner	Art Unit
	Frederick F. Krass	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 17 March 2004.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 11-13, 17 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 11-13, 19 and 21 is/are rejected.
- 7) Claim(s) 17 and 20 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/17/04; 1/27/05.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_.

### **Previous Rejections**

All previous rejections are hereby expressly withdrawn.

The current examiner agrees with the reasoning provided by Applicant in the Appeal Brief, substantially as written. USP 5,665,378 does not disclose the treatment of migraines. Instead, it treats menstrual cramps and muscular back pain, conditions etiologically unrelated to migraine. Gobel et al also does not specify the treatment of migraine headaches. Simply put, there is no motivation present for combining these references without using impermissible hindsight reconstruction based on Applicant's specification.

### **Claim Informalities**

The following amendment is suggested to place the claims in better form:

Claim 20, fifth line, "synergistically as" should be changed to --- as synergistically ---

### **New Matter Rejection**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support is seen in the specification as originally filed for synergistic (i.e., having greater than additive effect) combinations of l-menthol and juniper or rosemary oils. The specification as originally filed does not appear to disclose the broad concept of synergy; instead, it demonstrates same experimentally and then only for l-menthol in specific combination with peppermint, lavender and rose oils. See Tables 1 and 2 at pages 9 and 10 of the instant specification, respectively.

### **Obviousness Rejection**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 11-13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rucker ("Mint Oil Reduces Headaches", Translation of relevant parts of XP-001157330) in view of Hipskind et al (USP 5,792,760).

The primary reference discloses the use of peppermint oil in liquid form to reduce headache pain, by applying 10ml of a 10% solution to the forehead and temple, dividing the total dose into three single subdoses which are applied with an interval of 15 minutes between each. The reference states what is well-known in the art, namely that peppermint oil contains (l-) menthol as a main active component. It also states that peppermint oil "reduces headaches because it inhibits the effect of the two messengers serotonin and Substanz P", but differs from the instant claims insofar as it discloses the treatment of tension headaches, while remaining silent regarding migraines. (Note that the instantly rejected claims are read upon by the administration of peppermint oil alone, since when the oil is administered its active ingredient (menthol) is simultaneously administered as well. These claims as currently written do not provide any clear line of demarcation, e.g. specific proportions, between the menthol active ingredient and the oil which carries it. Note further that this is not the case with claims 20 and 21 since synergy requires two separate components. Nor is it the case with claim 17, wherein the term "respectively", coupled with the use of different range values, also requires separate components).

The secondary reference teaches that substance P is involved in the neurotransmission of pain sensations, including the pain associated with migraine headache, and thus can be treated with a substance P inhibitor. See col. 2, lines 32-43; col. 4, lines 20 and 21; col. 32, lines 55-66 and col. 44, lines 52 et seq. A preferred route of administration for the substance P inhibitor is transdermal, via patches to provide continuous or discontinuous infusion in controlled amounts. See col. 48, lines 3-12. The secondary reference differs from the instant claims, however, in that it discloses particular bisindoles as substance P inhibitors, rather than menthol as claimed instantly.

Since peppermint oil (l-menthol) is a substance P inhibitor as disclosed by the primary reference, it would have been obvious to have used it to treat migraine headaches as taught by the secondary reference. The motivation to do so would arise from sound scientific reasoning and the natural desire of physicians to expand the use of known therapies to as many patients as would reasonably be expected to benefit therefrom. Regarding instant claim 12, it would have been obvious to have used a patch to administer the topical liquids of the primary reference, motivated by the desire to provide improved control over administration as taught by the secondary reference.

2) Claims 11, 13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butler (USP 5,629,281).

The prior art discloses the treatment of headaches by administering a liquid containing peppermint (and thus l-menthol) and other oils to the scalp (i.e., upper forehead). See col. 1, lines 21-27. The reference does not appear not anticipatory *per se* insofar as the language describing the treatment of migraines at col. 1, lines 47-50 is suggestive, with migraines needing to be selected from a group of potentially treatable headache types, but it would have been obvious on its face to have treated migraines based on that unambiguous suggestion.

3) Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Butler (USP 5,629,281) in view of Hipskind et al (USP 5,792,760).

The primary reference is discussed in detail in subsection "2)" supra and differs from the instant claim insofar as it does not specifically disclose transdermal dosage forms, e.g. ointments or patches.

The secondary reference is discussed in detail in subsection "1)" supra and teaches that it is known to control transdermal administration with a patch. Accordingly, it would have been obvious to have used a patch to administer the topical liquids of the primary reference, motivated by the desire to provide improved control over administration as taught by the secondary reference.

### **Allowable Subject Matter**

Claims 17 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art of record does not fairly suggest, teach or disclose treating migraines by dermally administering a combination of 0.01-1% by weight menthol and 0.001-1% of an essential oil selected from the group consisting of lavender, juniper, peppermint, rosemary and rose oils, respectively. And, as demonstrated by the instant working examples, the combination of menthol and representative essential oils, respectively, provides unexpected efficacy in treating migraine headaches, a result which could not have in any way been predicted from the prior art of record.

Note that the amounts used by the instant Application (the amounts at which synergy is observed) are substantially lower than those used by the prior art. For instance, USP 5,665,378 uses amounts on the order of 15 to 40 percent (see col. 6, lines 28-35). The unexpected result of (synergistic) anti-migraine effectiveness at very low dosages observed by Applicant has self-evident advantages, e.g. it would be expected to provide lowered side effects, it would be less expensive, etc.

### **Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 10:30AM- 7PM;  
Tuesday: 10:30AM - 7PM;  
Wednesday: off;  
Thursday: 10:30AM- 7PM; and  
Friday: 10:30AM-7PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass  
Primary Examiner  
Art Unit 1614



<b>Notice of References Cited</b>		Application/Control No.	Applicant(s)/Patent Under Reexamination	
		09/890,552	YOKOYAMA ET AL.	
Examiner		Art Unit		Page 1 of 1
Frederick F. Krass		1614		

**U.S. PATENT DOCUMENTS**

*	Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
A	US-5,792,760	08-1998	Hipskind et al.	514/217.08
B	US-			
C	US-			
D	US-			
E	US-			
F	US-			
G	US-			
H	US-			
I	US-			
J	US-			
K	US-			
L	US-			
M	US-			

**FOREIGN PATENT DOCUMENTS**

*	Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
N					
O					
P					
Q					
R					
S					
T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

GMM/KJR/jao



Form PTO-1449

ATTY. DOCKET NO.  
0020-4883P

APPLICATION NO.  
09/890,552

**INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION**

(Use several sheets if necessary)

APPLICANT  
H. YOKOYAMA et al.

FILING DATE  
August 2, 2001

GROUP  
1614

**U. S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	KIND	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
	US						
	US						
	US						
	US						
	US						
	US						
	US						
	US						
	US						
	US						

**FOREIGN PATENT DOCUMENTS**

Office	DOCUMENT NUMBER	Kind	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
FK	EP 0 239 802	A3	10/7/1987	EP			X	

**OTHER DOCUMENTS** (Include Name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.)


EXAMINER	Krass, Frederick	DATE CONSIDERED
		2-18-05

EXAMINER: Initial if citation considered, whether or not citation is in conformance with M.P.E.P. 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

*Krass*  
GMM/KJR:kdm